REMARKS

Claims 13-24 stand pending in the present application. By this Second Preliminary Amendment, Applicants have amended claims 13-24 to correct inconsistencies presented in the pending application as filed, and to add an Abstract to the case on a separate page. This amendment does not constitute new matter based on the discussion which follows.

It was discovered during a further review of the present application that a clerical nomenclature error occurred when preparing the present application. In the present art, there are two different methods of referring to the same polymorphism. Hansen et al (incorporated by reference, Substitute Specification, ¶ 0018) and Inoue et al (*Diabetes*, Vol. 45, June 1996) use two different methods for referring to the same polymorphism. Provided herewith, Applicant has submitted an Information Disclosure Statement with said two references.

Hansen et al refers to the present *SUR1* gene using the nomenclature -3c→t whereas, Inoue et al refers to the same mutation as -3t→c. In further detail, Hansen et al (pages 599-600) identifies the 3 bp before intron/exon 16 boundary as equivalent to the previously termed variant in intron 24 identified by Inoue et al. Further, Hansen et al numbers exons consecutively in order from the 5' end of the gene, whereas, Inoue et al numbers exons from the 3' end of the gene. Thus, Hansen et al and Inoue et al both refer to the same polymorphism although using a totally different nomenclature.

Consistent with Hansen et al as stated in ¶ 0018 the *SUR1* gene of the present invention is intended to be according to the nomenclature of Hansen et al (see Substitute Specification, ¶ 12). Applicants do not elect to have identified a new

polymorphism. On the contrary, the present Applicants rely on the known polymorphism in *SUR1* gene to investigate the most frequent one. Therefore, one of ordinary skill in the art would readily recognize that a clerical nomenclature error occurred in the present application, since the polymorphism named "a -3t→c mutation located in intron 16, namely in position -3 of the exon 17 splice acceptor site" does not exist (strictly speaking) in the art. Moreover, no reference is made on such polymorphism in the art.

Indeed, because of these two ways of naming this polymorphism and of numbering the introns and exons on *SUR1* gene, the Applicants made inadvertent clerical errors in the naming of this most frequent polymorphism, by using the Inoue et al reversal nomenclature of "a -3t→c mutation" and by locating it on intron 16, whereas using the Hansen et al nomenclature, the mutation is actually on intron 15, i.e., 3 bp before the intron/exon 16 boundary. Consistent with this, the intron before the exon 16 is called intron 15 and not intron 16 as originally specified.

The only mutation stated by Hansen et al or Inoue et al (with the aforementioned differences of naming and of numbering it system) which can correspond to the one studied by the present inventors is the one termed: "-3bp intron/exon 16 boundary", also called by Hansen et al "a c→t intron variant in position -3 of the exon 16 splice acceptor site". Indeed, it is the described most frequent polymorphism on *SUR1* and it is the only one located in an intron, -3bp before an intron/exon boundary.

The present clerical nomenclature error of naming the polymorphism -3t→c as Inoue et al occurred when the present inventors analyzed their results by typing the

so-called intron 16 -3t→c polymorphism described in Inoue et al as stated in ¶ 0044 (Substitute Specification).

Consequently, the Applicants named the allele to be detected -3c (instead of -3t), as to be consistent with the error of naming the polymorphism "-3t→c" (instead of -3c→t). Therefore, each time the Applicants referred to -3c in the original specification, it should have been -3t. Moreover, when stating that "the presence of at least one -3c allele identifies a NIDDM patient with a higher susceptibility toward sulfonylurea therapy", it should also have been "the presence of at least one -3t allele identifies a NIDDM patient with a higher susceptibility toward sulfonylurea therapy.

In order to correct the nomenclature clerical error and to be consistent with the nomenclature of Hansen et al as stated in the present application, Applicants have amended the present application including the specification, claims and abstract by replacing reference to a -3t→c mutation located in intron 16, namely in position -3 of the exon splice acceptor site with reference to a -3c→t mutation located in intron 15, namely in position -3 of the exon 16 splice acceptor site. Further, reference to "detecting -3c allele" has been corrected to "detecting -3t allele" and therefore, "the presence of at least one -3c allele identifying an NIDDM patient with a high stability towards sulfonylurea therapy" has been corrected to detecting the "presence of at least one -3t allele" which identifies a NIDDM patient with a high susceptibility towards sulfonylurea therapy.

The aforementioned correction of naming the polymorphism -3→t from -3t→c is obvious to one of ordinary skill in the art from the present specification and prior art incorporated therein.

First, in view of Hansen et al, the "c→t intron variant in position -3 of the exon 16 splice acceptor site" is the same as the one called by Inoue et al "intronic -3t→c change located at the intron 24 splice acceptor site" (see on the top of page 600 of Hansen et al).

Second, Inoue et al state that when a change of -3t into -3c occurs, a Pst1 site is destroyed (see page 828, ¶ 3). This phrase makes no sense, since one of ordinary skill in the art knows that the Pst1 restriction enzyme specifically recognizes the CA/G sequence and cleaves on the / location thereof. Accordingly, either Inoue et al made an error on the sense of the mutation or on the term "destroy". Referring to Hansen et al, when the amplified exon 16 (nt-3) products were digested by Pst1 restriction enzyme, it is stated that the exon 16 (nt-3) fragments obtained therefrom were as follows: wild-type: 164 and 38bp; heterozygous: 202, 164, and 38bp; and homozygous: 202bp (see Hansen et al, page 601, left column). This clearly means that the wild-type corresponds to the cc genotype (cleavage with Pst 1) and the homozygous to the tt genotype (no cleavage with Pst 1). By combining this technical teaching with the disclosure of Inoue et al, one of ordinary skill in the art readily concludes that Inoue actually made an error on the sense of the mutation and not on the term "destroy", i.e., the correct way of naming this polymorphism is -3c→t.

In view of the foregoing, Applicants respectfully submit that the present Preliminary Amendment merely corrects clerical deficiencies and/or nomenclature inconsistencies in the present application and therefore does not constitute new matter. Moreover, the amendment places the present application in a better condition for examination.

Favorable consideration of the above request, and examination and allowance of this application is thus earnestly solicited.

Respectfully submitted,
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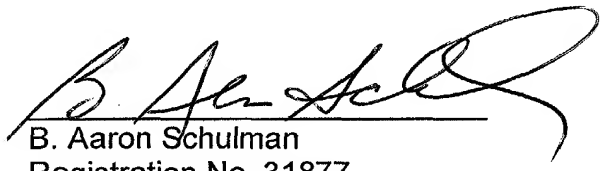

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